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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/227,518	01/08/99	TERRY B	5441.200-US

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1641	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/227,518	Applicant(s) TERRY ET AL.	
	Examiner Gailene R. Gabel	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-38* is/are pending in the application.

4a) Of the above claim(s) *17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *17-38* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 8/6/01 in Paper No. 11 is acknowledged and has been entered. Claims 1-16 have been cancelled. Claims 18-38 have been added. Currently, claims 17-28 are pending. Claims 18-28 are under examination.

Rejections Rendered Moot

Claim Rejections - 35 USC § 112, 102, and 103

2. The rejection of claims 1-16 under 35 U.S.C. 112, 102, and 103 are now moot in light of Applicant's cancellation of the claims.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 18-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is indefinite in reciting, "array of test compounds held on a solid support" because it is unclear what is encompassed by "held on a solid support" as

used in the claim". For example, are the test compounds attached or coated on wells of a solid support. Alternatively, does the solid phase comprise or include a porous membrane or a non-porous substrate.

The term "such that" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. Language such as, "wherein" may obviate this rejection.

Claim 18 is indefinite in failing to clearly establish a relationship between the test compound and the bioactive compound. For example, is a response indicative that the test compound is a bioactive compound.

Claim 21 lacks antecedent support in reciting, "the preceding claims".

Claim 26 is indefinite in failing to clearly establish a relationship between the "non-porous substrate" in claim 18 and the "an optically clear substrate" in the instant claim.

Claim 27 has improper antecedent basis problem in reciting, "A method according to claim ...".

Claim 27 is indefinite in reciting, "held on a porous membrane or a non-porous substrate" because it is unclear what is encompassed by "held" as used in the claim".

Claim 27 has improper antecedent basis problem in reciting, "a porous membrane or a non-porous substrate".

Claim 28 has improper antecedent basis problem in reciting, "A method according to claim ...".

Claim 28 is indefinite in failing to clearly establish a relationship between the "localized liquid which is in contact with the detector layer" in claim 18 and the "a liquid layer overlaying the detector layer" in the instant claim. Alternatively, claim 28 has improper antecedent basis problem in reciting "a liquid layer".

Claim 30 is indefinite in reciting, "test compounds are held on a solid support" because it is unclear what is encompassed by the term "held" as used in the claim". For example, are the test compounds attached or coated on wells of a solid support.

Claim 30 has improper antecedent basis problem in reciting "a solid support".

Claim 31 has improper antecedent basis problem in reciting "a porous membrane".

Claim 32 lacks antecedent support in reciting "the field of view of".

Claim 33 lacks antecedent support in reciting "the field of view of".

Claim 32 has improper antecedent basis problem in reciting "an optical detector".

Claim 36 is indefinite in reciting, "generated on the solid support" in relation to claim 18 which recites that the test compounds are "held" on the solid support. Please clarify. See also claim 19.

Claim 38 is ambiguous in reciting, "the test compounds are viral or bacteriophage particles ... to display compounds upon their surfaces" because it is unclear what is encompassed by the term "compounds" in the second occurrence of the claim in relation to its first occurrence.

Claim R jections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

4. Claims 18-19, 21, 23-25, and 24-25 (34-35) are rejected under 35 U.S.C. 102(b) as being anticipated by Sittampalam et al. (Current Opinion in Chemical Biology, 1997).

Sittampalam et al. teach cell based assay systems for use in high throughput screens wherein physiologically viable cells are coated onto a detector layer made from scintillant plastic so that upon contact with a test compound, the cells are monitored for bioactivity (cellular events, cytosolic calcium mobilization) (see page 365, column 1). The scintillant plastic is incorporated on 96 microwell plates wherein its surface is able to function as a pH sensing surface or a temperature sensing surface (see page 386, column 2). Sittampalam et al. also teach that illumination systems such as FRET systems are capable of exciting fluorescence of the detector layer and detecting changes in fluorescence or luminescence properties of the cells (see page 388, column 1). Sittampalam et al. teach that the most common method for detecting ligand interaction between test compounds (drugs) and targets in cells is to employ reporter genes.

5. Claims 18-19, 21, and 34-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Isacoff et al. (US 5,756,351).

Isacoff et al disclose a method for monitoring the physiological status of a cell. Specifically, Isacoff et al. disclose a method for screening test compounds for bioactivity (different cellular states, ligand binding, changes in distribution cross plasma membrane) using biomolecular optical sensors (see column 1, lines 35-58 and column 16-34). Isacoff et al. specifically disclose contacting an array of test compounds with a detector layer comprising physiologically viable cells which produces a detectable response (different signals) which is indicative of bioactivity. The detectable response results from a change in fluorescence or luminescence property of the cells (see column 2). Detection is determined with an illumination system (luminescer generating system) which that is capable of exciting fluorescence or luminescence of the detector layer using selected wavelengths with defined order or time of duration (see column 1, lines 58-67 and column 3, lines 9-14).

6. Claims 18-22, 26, 32-33, 34-35, and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Negulescu et al. (US 6,214,563).

Negulescu et al. disclose cell-based assays for use in drug discovery to screen large numbers of test compounds for bioactivity. Negulescu et al. specifically disclose contacting an array of test compounds with a detector layer that is comprised of physiologically viable cells (membrane compartments=cells) that are in physical and optical contact with a sensing surface (solid phase) (see column 3, lines 10-16 and

column 5, lines 48-53). The viable cells on the detector layer preferably form a monolayer (single layer) (see column 14, lines 5-10). Negulescu et al. also disclose a sample distribution module wherein sample (test compound/chemical) from the sample surface (chemical well) is transported for contact with the cellular detector layer during the course of measurement (see column 17, lines 24-28). Alternatively, the cells from the detector layer can be contacted with the test compounds in chemical wells (see column 21, line 61 to column 22, line 8). The detection step uses different fluorescent monitoring systems including those adapted to high throughput screening such multi-well platforms (see column 16, line 63 to column 17, line 3 and lines 44-47). If the test compound has bioactivity as a candidate modulator, there is a change in the fluorescence or luminescence property of the cellular detector layer which is determined by an illumination system by exciting the fluorescent reporter on the detector layer with various selected wavelengths (see columns 22 and 23).

7. Claims 18, 21-23, 27-33, and 36-37 are rejected under 35 U.S.C. 102(e) as being anticipated by Chelsky et al. (US 5,856,083).

Chelsky et al. disclose a lawn assay for screening and determining test compounds that are held on porous or non-porous solid support (see column 3, lines 30-67, column 5, lines 15-52, and column 6, lines 62-67). Chelsky et al. specifically teach that the test compounds are linked to the support by a cleavable linker and upon cleavage of the linker, the test compounds diffuse into a support's vicinity comprising a colloidal matrix or a scintillant coated surface so that high concentrations of the test

compounds are created on these supports (see column 3). Compounds released are then contacted with cellular receptors, i.e. membrane bound receptors on the scintillant supports so that binding interaction therebetween can be detected and measured using a fluorescence detection and illumination systems (see column 4, specifically lines 51-61). Chelsky et al. teach application of the invention in combinatorial libraries and drug discovery assays.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sittampalam et al. (Current Opinion in Chemical Biology, 1997) or Chelsky et al. (US 5,856,083).

Sittampalam et al. and Chelsky et al. have been discussed supra. Sittampalam et al. and Chelsky et al. differ in failing to teach viral and bacteriophage particles as test compounds in an array.

However, the viral and bacteriophage particles recited in claim 38 constitute obvious variations of species which are routinely varied in the art and which have not been described as being critical to the practice of the invention.

Response to Arguments

9. Applicant's arguments filed 8/6/01 have been fully considered but they are not persuasive.

A) Applicant argues that the claimed method uses a well-less system for simultaneous screening of large numbers of test compounds for biological activity which avoids the complications of dispensing multiple microvolumes of many different fluids. Applicant argues that Sittampalam teaches a 96 well format which suggests using pipetting to dispense the test compounds.

In response, claim 18, as currently recited, recites a solid support which does not exclude the 96 well format of Sittampalam.

B) Applicant argues that Isacoff does not teach a well-less system.

In response, claim 18, as currently recited, recites a solid support which does not exclude the system or format taught by Isacoff.

C) Applicant argues that Negulescu fails to teach a well-less system and teaches that the test compounds are in solution.

In response, claim 18, as currently recited, recites 1) a solid support which does not exclude the system or format taught by Negulescu and 2) an array of test compounds which does not exclude test substances in solution as taught by Negulescu.

D) Applicant argues that the solid supports taught by Chelsky are beads containing compounds which can be incorporated into a gel, i.e. colloidal matrix such as agarose. Applicant further argues that Chelsky does not teach an array of compounds held on a single solid support and a sensing layer comprising living cells. Therefore, Applicant contends that there is no suggestion or motivation to combine Chelsky with Sittampalam or Negulescu in order to lead to the present invention.

Applicant's arguments with respect to the combination of Sittampalam or Negulescu with Chelsky have been considered but are moot in view of the new grounds of rejection.

In response to Applicant's argument on the teaching of Chelsky, it is said that the rejected claims are anticipated by Chelsky in teaching the use of a well-less system, a porous membrane in the form of colloidal matrix or any other matrix that allows diffusion of test compounds into its matrix in order to screen for bioactivity in a lawn assay.

Chelsky also teaches attaching the test compounds into non-porous substrate or controlled pore-glass beads (see column 6, lines 61-67).

10. No claims are allowed.

11. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday from 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
October 18, 2001

LONG V. LE
SUPERVISORY PATENT EXAMINER
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10/22/01